Orthopaedics & Traumatology: Surgery & Research xxx (xxxx) xxx

Contents lists available at ScienceDirect

Orthopaedics & Traumatology: Surgery & Research

journal homepage: www.elsevier.com

Original article

Selective pathological examination following hip arthroplasty: A retrospective cohort study

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ARTICLE INFO

Article history:
Received 9 March 2020
Accepted 30 November 2020
Available online xxx

Keywords:
Hip
Femur head
Arthroplasty
Pathology
Pathological examination

ABSTRACT

Background: Pathological examination of the femoral head after hip arthroplasty is often performed routinely. The cost-effectiveness of the examination with regard to identifying clinically relevant diagnoses has been a point of discussion. To date, recommendations on performing pathological examination based on patient characteristics, disease history or radiographic findings are scarce. The aim of this study was to gain insight in when to select a patient for pathological examination of the femoral head by means of the following research questions: "How many clinically relevant diagnoses does selective pathological examination identify?" "Which factors contribute to selection of the femoral head for conducting pathological examination?" "What are the costs of selective pathological examination for identifying clinically relevant diagnoses?"

Hypothesis: Selective pathological examination of the femoral head results in higher ratios of identified clinically relevant diagnoses against substantially lower costs.

Methods: A retrospective cohort study was performed over the period of 2010–2015. All pathological reports were collected from our hospital and screened for resected femoral heads after primary total hip arthroplasty (THA) or primary hemiarthroplasty (HA). The coherence between preoperative diagnosis and postoperative pathological diagnosis was defined as concordant, discrepant or discordant. The aim was to perform logistic regression analysis.

Results: In total, 164 patients were included of 3998 hip arthroplasties performed during the study period with a mean age of 74 ± 12.3 years including 54 (33%) male and 110 (67%) female of whom 112 (68%) underwent THA and 52 (32%) HA. A discrepancy in diagnosis was found in nine patients (6%) and discordance in three patients (2%). The most frequently reported reasons to perform pathological examination were malignancy in medical history $n = 86$ (53%), avascular necrosis $n = 22$ (13%), bone abnormality perioperatively $n = 19$ (11%) and pathological fracture $n = 13$ (8%). The factors that identified the unexpected clinically relevant diagnoses were pathological fracture (3 cases out of 13), bone abnormality perioperatively (2 out of 19), abnormalities on preoperative radiographs (1 out of 9) and to a lesser extent malignancy in history (2 out of 86). With costs of pathological examination of approximately €163 per femoral head, performed in 164 patients, the total costs of pathological examination resulted in €26,732. The cost per discrepant case ($n = 9$) was €2970 and the cost per discordant case ($n = 3$) was €8910.

Conclusion: Selective pathological examination of the femoral head following hip arthroplasty results in higher ratios of discrepant and discordant cases against substantially lower costs. Factors that identify clinically relevant diagnoses are pathological fracture, perioperative bone abnormality, abnormalities on preoperative radiographs and to a lesser extent malignancy in history.

Level of evidence: III; retrospective cohort study.

1. Introduction

Total hip arthroplasty (THA) and hemiarthroplasty (HA) are among the most common orthopaedic surgical procedures in the

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https://doi.org/10.1016/j.otsr.2021.102942
1877-0568/

Please cite this article as: B.A. Schermer, M.R. Bénard, L.J. Kleeblad et al., Selective pathological examination following hip arthroplasty: A retrospective cohort study, Orthop Traumatol Surg Res, https://doi.org/10.1016/j.otsr.2021.102942

Western countries, counting more than 420,000 annually in the United States of America (USA) [1]. During these procedures, the femoral head is resected and historically, there was a common practice of routine pathological examination of the femoral head [2–4]. Despite a decrease in pathological examination of the femoral head from 50% in 2006 to 45% in 2016, still 35% of hospitals in the USA utilize histopathology in 91–100% of THA cases [5].

Arguments in favor of routine analysis are to obtain more knowledge of tissue, perform quality assessment for bone banking and detect unexpected malignancies which may affect patient's health [3,4,6–11]. A discrepancy in diagnosis between pre- and postoperative pathological result has been reported, with a discrepancy rate ranging from 1–8.9% [2–4,6–9,11–17] implying pathological examination can lead to more knowledge of tissue, which can be helpful in future diagnosis and treatment. Additionally, a study performed in a center with more osseous histologic experience conducting more comprehensively examination of joints and synovial tissues reported a discrepancy rate between preoperative and postoperative pathological diagnosis of 18.8% in 7968 total hip replacements [8]. Also, routine pathological examination of femoral head may be cost-effective with a cost-utility ratio of $49,570/QALY (Quality Adjusted Life Years) gained, which is below the World Health Organization (WHO) recommend threshold of $159,000/QALY gained [7]. In contrast, others reported that routine pathological examination is not cost-effective due to the low prevalence of unexpected findings and the fact that patient treatment is rarely altered [12,13,17].

To the best of our knowledge, there are no uniform guidelines with regard to pathological examination of the resected femoral head following THA or HA. With contrasting viewpoints concerning the motives to perform the analysis, decisions are based mostly on hospital protocol [5]. In a large national database study, it was found that 40% of all femoral heads sent to the pathologist came from hospitals that utilized histopathology only in 1–10% after THA [5]. To date, there have been some reports suggesting to perform pathological examination only in a selected group of patients [12–16,18,19]. However, clear guidelines for when to select a patient for pathological examination of the femoral head are absent with only one report actually describing factors that should lead to pathological examination, namely: no clear history of trauma or malignancy suspicion on radiological findings [19]. Though, this study was performed only in patients with femoral neck fractures that were suspected for malignancy and underwent HA.

Therefore, a retrospective analysis was performed to assess the potential necessity of performing pathological examination of surgically resected femoral heads following THA or HA in a selected group of patients. It could be cost saving for the health care system to perform pathological examination selectively [2,14–17]. The aim of this study was to gain insight in how many clinically relevant diagnoses were found with selective pathological examination and which factors identified them. Hereby taking into account patient characteristics and medical history, radiographic findings and bone aspect perioperatively. The research questions were:

- How many clinically relevant diagnoses does selective pathological examination identify?;
- Which factors contribute to selection of the femoral head for conducting pathological examination?;
- What are the costs of selective pathological examination?

We hypothesized that performing pathological examination of the femoral head in a selected group of patients results in higher ratios of discrepant and discordant cases against substantially lower costs.

Table 1
Demographic characteristics and reported reasons to perform pathological examination.

Gender	54 (32.9%) male, 110 (67.1%) female
Mean age	74.1 ± 12.3 years
Mean BMI	25.5 ± 3.9 kg/m^2
Side (right : left)	91 (55.5%) : 73 (44.5%)
Type of surgery	112 (68.3%) THA, 52 (31.7%) HA
Reason for pathological examination	
Malignancy in history	86 (53%)
Avascular necrosis	22 (13%)
Bone abnormality perioperatively	19 (11.5%)
Pathological fracture	13 (8%)
Synovitis/inflammation	10 (6%)
Abnormalities on radiograph	9 (5.5%)
Paget's disease	2 (1%)
Other	3 (2%)

BMI: body mass index; THA: total hip arthroplasty; HA: hemiarthroplasty.

2. Methods

2.1. Data collection

A retrospective cohort study was performed over the period of 2010–2015. In our hospital, whether to perform pathological examination of the resected femoral head or not is decided by the individual orthopaedic surgeon. After the local hospital board approved the study, all pathological reports were collected from the department of pathology of the Alrijne Hospital, Leiderdorp, the Netherlands. All reports from 2010 to 2015 were screened for terms of hip, femoral, head, bone or joint. This resulted in 298 reports (Fig. 1). These reports were checked for inclusion using the inclusion criteria: 1) resected femoral head during primary THA or HA; 2) known medical history of the patient; and 3) known reason for sending the femoral head for pathological examination. Exclusion criteria were: 1) previous hip surgery on the ipsilateral side; and 2) a pathology report containing material from elsewhere in the body (i.e. not the femoral head). This resulted in 164 patients for inclusion of which 54 (33%) were male and 110 (67%) were female (Table 1). The mean age was 74.1 ± 12.3 years with a mean BMI of 25.5 ± 3.9 kg/m^2. The distribution of THA and HA was 112 (68%) versus 52 (32%).

All patient data was collected including gender, age, BMI, side of operation, preoperative diagnosis, reason for pathological examination, result of pathological examination, nature and year of diagnosis of primary tumor, classification of tumor, metastatic disease and treatment. The most frequent reasons for the orthopaedic surgeons to send the femoral head to the pathologist were malignancy in medical history (53%), avascular necrosis (13%), bone abnormality perioperatively (11%) and pathological fracture (8%) (Table 1).

2.2. Pathological examination

Pathological examination was performed according to protocol, based on Rosai and Ackerman's surgical pathology with extended sampling [20]. Directly following surgery, the specimen was put into 4% formaldehyde solution for initial fixation. The specimen was conserved in formaldehyde until further processing. A minimum of 16 hours was required for the initial fixation, then the femoral head was examined macroscopically for irregularities of the surface or plane of resection. Subsequently, the specimen was cut manually resulting in a 4 mm thick central true cut sample of the femoral head. Sections were further fixated for 24 hours in 4% formalin solution and then decalcified in Decalcifier Solution (Dako, Agilent Pathology Solutions, CA, USA) until fit for further processing to histological slides. When the sample contained any lesions

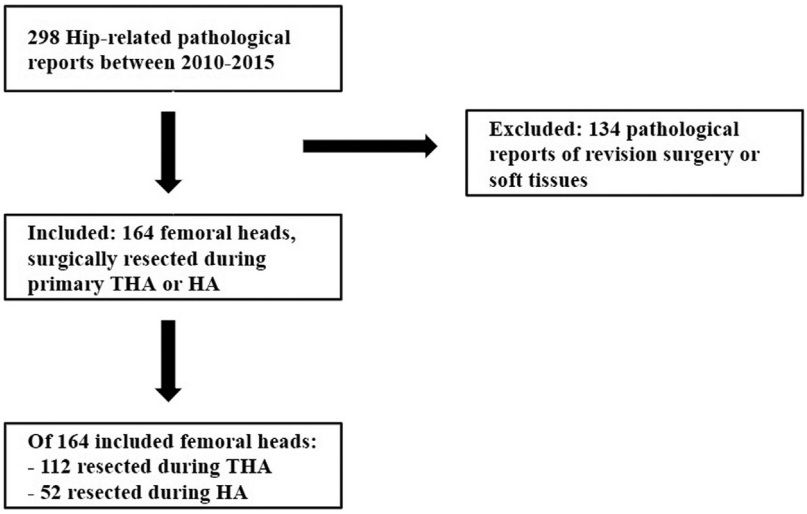

Fig. 1. Flowchart of inclusion and exclusion (THA: total hip arthroplasty; HA: hemiarthroplasty).

suspicious for malignancy at macroscopic examination, additional samples were taken and decalcified in Oxford fixate (formaldehyde, sodium chloride, acetic acid and zinc acetate) for better morphology. In case of lesions with a microscopically visible substrate, the Oxford fixate solution facilitates immuno-histochemical staining if necessary for further classification. The histologic slides were routinely evaluated microscopically by one pathologist with the possibility of internal and external consultation. The costs to perform pathological examination in our hospital are €163 per femoral head.

2.3. Methods of assessment

The coherence between preoperative diagnosis and postoperative pathological diagnosis is described as concordant, discrepant or discordant [2,7,8,12,13,16,17]. Concordant is defined as no difference in preoperative and postoperative pathological diagnosis; discrepancy as a difference in preoperative and postoperative pathological diagnosis with no alteration in treatment and discordance as a difference in preoperative and postoperative pathological diagnosis with alteration in treatment such as adjuvant chemo- or radiotherapy. Also, factors that identified unexpected clinically relevant diagnoses were clarified and preoperative radiographs from these unexpected diagnoses were reviewed. Furthermore, a cost per discrepant case and a cost per discordant case was calculated by dividing the total costs of pathological examination for our study cohort by the number of discrepant and discordant cases. The total cost of pathological examination was calculated at the average of €163 per femoral head in our hospital multiplied by 164 patients in our study cohort resulting in €26,732.

2.4. Statistical analysis

The clinical details including gender, age, BMI, date of surgery, indication for and type of hip arthroplasty and reason for pathological examination were assessed using descriptive statistics consisting of mean and standard deviation, and frequencies reported as percentages or ratios using IBM SPSS software version 26. To study the factors that identify unexpected clinically relevant diagnoses the occurrence of the relevant parameters were expressed as ratio to the clinically relevant cases. The aim was to perform logistic regression analysis.

3. Results

The pre- and postoperative diagnoses by type of hip arthroplasty are shown in Table 2. The most common preoperative diagnosis was osteoarthritis (82.1%) for THA and fracture (82.7%) for HA whereas the postoperative diagnosis was osteoarthritis for THA in 80.4% and fracture for HA in 65.3% of patients. In the THA group, eleven cases appeared to have a pathological report concluding only “osteoporotic features”; however, after reviewing these cases the diagnosis was considered to be osteoarthritis based on clinical findings, preoperative radiographs and perioperatively bone aspect.

In total, 152 of 164 (92.7%) pathological diagnoses were concordant with the preoperative diagnosis (Table 3). In nine cases (5.5%), the pathological diagnosis showed discrepancy with the preoperative diagnosis. The most common reason for discrepancy was when avascular necrosis was suspected on the preoperative radiograph, but pathological examination showed osteoarthritis ($n = 6$). In the other three cases, one case of osteomyelitis was found (in a patient who underwent three lavage and debridement procedures of THA due to infection), but not treated for the osteomyelitis itself, and one case of ochronosis was discovered after reviewing the pathological specimen due to atypical black pigmented bone aspect found during total knee arthroplasty one year after THA. Both bone diseases were found after pathological examination was performed because of perioperatively bone abnormality in combination with synovitis.

Discordance was found in three cases (1.8%, Table 4). The first discordant case was a patient undergoing THA with lung cancer in recent medical history showing metastatic bone disease after pathological examination of the femoral head. Clinically this patient had a pathological fracture, however on the radiograph of the hip, there were no lytic lesions and PET-CT declared no signs of skeletal metastasis. Furthermore, perioperatively no signs of metastasis were identified. The second discordant case was a patient with a history of pulmonary metastatic sigmoid carcinoma for which sigmoid colectomy was performed four years prior to the HA with a pathological report showing metastasis in the femoral head. Clinically this patient had a pathological fracture, however neither on the radiograph of the hip nor perioperatively signs of metastasis were identified. The third discordant case was a patient with a pathological fracture in which small cell B-cell lymphoma was diagnosed after HA, despite the absence of a definitive diagnosis after earlier lymph node biopsy the suspicion of a lymphoma was high on preoperative PET-CT. The radiograph of the hip indicated

Table 2
Preoperative diagnosis and postoperative diagnosis following pathological examination by type of hip arthroplasty.

Type of arthroplasty	Diagnosis	Preoperative	Postoperative
THA ($n = 112$)	Osteoarthritis	92 (82.1%)	90 (80.4%)
	Avascular necrosis	10 (8.9%)	9 (8.0%)
	Fracture	5 (4.4%)	3 (2.7%)
	Pseudarthrosis	1 (0.9%)	1 (0.9%)
	Pathological fracture	1 (0.9%)	–
	Impending pathological fracture	2 (1.8%)	–
	Bone metastasis	–	5 (4.4%)
	Multiple myeloma	–	1 (0.9%)
	Osteomyelitis	–	1 (0.9%)
	Fibrous dysplasia	1 (0.9%)	1 (0.9%)
	No abnormalities	–	1 (0.9%)
HA ($n = 52$)	Osteoarthritis	–	7 (13.5%)
	Avascular necrosis	2 (3.8%)	2 (3.8%)
	Fracture	43 (82.7%)	34 (65.3%)
	Pathological fracture	4 (7.7%)	–
	Impending pathological fracture	3 (5.8%)	–
	Bone metastasis	–	5 (9.6%)
	Multiple myeloma	–	3 (5.8%)
	Lymphoma	–	1 (1.9%)

THA: total hip arthroplasty; HA: hemiarthroplasty.

Table 3
Coherence between preoperative and postoperative diagnosis.

	Number of cases	Type of arthroplasty	%
Concordant	152		92.7%
Discrepant: pre–post	9		5.5%
Avascular necrosis–osteoarthritis	6	THA ($n = 6$)	3.7%
Osteoarthritis–no abnormalities	1	THA	0.6%
Osteoarthritis–ochronosis	1	THA	0.6%
Osteoarthritis–osteomyelitis	1	THA	0.6%
Discordant: pre–post	3		1.8%
Pathological fracture–bone metastasis	1	THA	0.6%
Pathological fracture–B-cell lymphoma	1	HA	0.6%
Pathological fracture–bone metastasis	1	HA	0.6%

THA: total hip arthroplasty; HA: hemiarthroplasty.

Table 4
Characteristics of the discrepant and discordant cases with clinically relevant postoperative diagnoses.

Type	Preoperative diagnosis	Type of arthroplasty	Postoperative diagnosis	Pathological fracture	Malignancy in history	Bone abnormality perioperatively	Abnormalities on radiograph
Discrepant cases	Osteoarthritis	THA	Osteomyelitis	No	No	Yes	No
	Osteoarthritis	THA	Ochronosis	No	No	Yes	No
Discordant cases	Pathological fracture	THA	Bone metastasis	Yes	Yes, lung cancer	No	No
	Pathological fracture	HA	B-cell lymphoma	Yes	No	No	Yes
	Pathological fracture	HA	Bone metastasis	Yes	Yes, sigmoid carcinoma	No	No

THA: total hip arthroplasty; HA: hemiarthroplasty.

a possible lytic skeletal lesion in the femoral head, however, no signs of bone metastasis were found on PET-CT. Despite a definitive diagnosis after pathological examination, the patient declined further investigation and treatment. After reviewing the PET-CT scans with a nuclear medicine physician no bone metastasis could be identified. This was explained by the fact that the fractures caused increased fluorodeoxyglucose activity and no skeletal metastasis was identified elsewhere due to a solitary metastasis.

The factors that identified the unexpected clinically relevant diagnoses were pathological fracture (3 cases out of 13), bone abnormality perioperatively (2 out of 19), abnormalities on radiographs (1 out of 9) and to a lesser extent malignancy in history (2 out of 86).

With 164 (4%) selected femoral heads of 3998 hip arthroplasties performed in our hospital during the study period, 3834 femoral heads were not examined. In combination with costs of approximately €163 per femoral head, this resulted in an estimated saving of €625,000 over our study period by performing pathological examination selectively. With total costs of pathological examination of €26,732, the cost per discrepant case in our study is €2970 and the cost per discordant case €8910.

4. Discussion

To date recommendations on performing pathological examination of the femoral head after hip arthroplasty based on patient characteristics, disease history or radiographic findings are scarce. One study reporting on factors that should lead to selection for pathological examination declares that no clear history of trauma and suspicion of malignancy on radiological findings may require additional investigation [19]. The aim of our study was to gain insight in how many clinically relevant diagnoses were found after

selectively performed pathological examination of the femoral head following THA and HA and which factors identified these diagnoses. The hypothesis that selective pathological examination of the femoral head results in higher ratios of discrepant and discordant cases against substantially lower costs was confirmed. In our pre-selected study population of 164 patients out of 3998 patients undergoing THA or HA, a discrepancy between pre- and postoperative diagnosis was found in 5.5% and discordance in 2%. Factors that identified clinically relevant diagnoses were pathological fracture, perioperative bone abnormality, abnormalities on preoperative radiographs and to a lesser extent malignancy in history.

Currently, still 35% of hospitals in the USA utilize histopathology in 91–100% of femoral heads retrieved from THA [5]. In our hospital, no routine pathological examination is performed, but a selection is made based on medical history, abnormalities on radiographs and perioperative bone abnormalities. Other studies have assessed routine pathological examination and noted lower ratios of discrepant and discordant cases [7,9,13,17]. Mackie et al. included 6161 femoral heads in which thirteen (0.2%) clinically relevant diagnoses were identified including eight confirmed neoplasms [9]. Liow et al. found a discordance rate of 5 out of 3200 (0.2%) with identifying three unexpected malignancies [7]. Two other studies reported on selective pathological examination of the femoral head after femoral neck fractures: Davis et al. found 2 unexpected neoplasms out of 466 selected patients (0.4%) with no alteration in treatment; Karuppiah et al. found 9 newly diagnosed malignancies out of 119 patients (7.5%) [18,19]. The latter study however only included patients suspected for malignancy, which could have caused the higher rate of unexpected findings. The findings of five clinically relevant diagnoses including three cases with bone metastasis in all 3998 hip arthroplasties performed in our hospital is comparable to previous studies, however against substantially lower costs. DiCarlo et al. found a considerably higher discrepancy and discordance rate in their routine pathological examination of respectively 18.8% and 5.4% in 7968 total hip replacements [8]. Their study was performed in a center with more osseous histologic experience conducting more comprehensively examination of joints and synovial tissues conceivably leading to higher rates of discrepancy and discordance. Selectively performed pathological examination identifies around 3% clinically relevant diagnoses based on the results of this study. The fact that malignancy in history only identified unexpected diagnoses in 2 out of 86 patients correspond with findings of Karuppiah et al. who concluded that history of malignancy alone is not an indication to perform pathological examination [19].

Concerning the cost-effectiveness of routine pathological examination of the femoral head, Liow et al. concluded that it might be cost-effective in the early detection of unsuspected malignancies. They calculated a cost-utility ratio of $49,569.74/QALY gained, which is below the WHO recommended threshold of $159,000/QALY gained [7]. In contrast to these findings, Lin et al. and Rubin et al. found no discordant cases in their cohorts, concluding that routine pathological examination is not cost-effective as an alteration in treatment is rare [13,17]. These cost-effectiveness studies showed around the same costs per discrepant and discordant case, though the difference in conclusion is due to the usage of different thresholds regarding cost-effectiveness. Previous studies found a cost per discordant case of around $122,000 when performing routine pathological examination [7,12]. In our study, selectively performed pathological examination resulted in a cost per discrepant case of €2950 and a cost per discordant case of €8900. Hypothetically, if only patients' femoral heads were selected that correspond to the factors that appear to identify the clinically relevant diagnoses (Table 4), so to create an optimal selection cohort, the number of patients in such cohort would be 137. With the findings of three discordant cases this results in an estimated cost per discordant case of €7450. Next to a substantially lower cost per discordant case, performing pathological examination only in certain cases can be cost saving on population basis [2,14–17]. Therefore, selective pathological examination of the femoral head following THA or HA may be preferable when taking into account the costs.

Our study has some limitations. Due to the selection of femoral heads by the individual orthopaedic surgeon, instead of routinely submitting all femoral heads to pathological examination, our study found substantially more unexpected malignancies in a much smaller group of patients. Consequently, this study is subjected to selection bias, though it serves the study's purpose of gaining insight in which factors have led to the selection for pathological examination. Note that this could lower the external validity of our study. Another limitation is the design of the study since it is retrospective and without a control group. Since there is no control group, it is unclear if clinically relevant diagnoses among the patients whose femoral head was not send to the pathologist were missed. However, this does not jeopardize the results of the study since the aim was to find out how many clinically relevant diagnoses were found with our selection and on which basis this selection was made. Another limitation is the relatively small sample size. This was due to the small number of selected cases in the study period of six years of collecting femoral heads after hip arthroplasty. Even in this selective group of patients, unexpected outcomes are uncommon. Due to the small number of discordant cases logistic regression could not be performed to build a proper model. Finally, this study did not include an estimation of patient's health benefits through the selective pathological examination, nor did we perform a cost-effectiveness analysis, as this was not the aim of our study. To our knowledge, this is the first study that aimed to gain insight in when to select a patient for performing pathological examination after THA or HA. Further studies should be conducted to evaluate which factors play a role in selecting patients to perform pathological examination of the femoral head following hip arthroplasty.

5. Conclusion

The findings of three malignant bone diseases and two non-malignant bone diseases imply that selectively performed pathological examination was effective and relevant. Next to substantially lower costs per discrepant and discordant case, performing pathological examination only in certain cases can be cost saving on population basis. Therefore, we recommend performing pathological examination selectively, especially in cases with a pathological fracture, perioperative bone abnormality, abnormalities on radiographs and to a lesser extent malignancy in history.

Disclosure of interest

The authors declare that they have no competing interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Contribution

BS, MB and JK wrote the manuscript. BS, MG and RM analyzed the data. MB and RM designed the study. All authors contributed to critical evaluation of the data and analyses, and critical revision of the manuscript.

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